

whereas "prior" is defined as "earlier in time or order." Thus, by their very definitions, these terms are mutually exclusive and one cannot be said to "indicate" the other.

The Examiner is also respectfully reminded that two of the applications parent to the present application (Serial Nos. 555,377 and 696,960) were allowed over the Balazs reference, primarily on the basis of the limitation that the coating was applied to surfaces involved in surgery prior to manipulation of tissue.

In Balazs, the solutions are applied or instilled, in every case, only after surgery has begun or has been completed. Note the procedure described in column 8, line 35 to column 9, line 65 of Balazs, wherein it is stated that only after "performing a temporal canthotomy," "extending the skin excision," "exposing the orbital bone," "dissecting skin and tissue free from the bone," "cutting a...piece of bone away," "excising conjunctiva and freeing it from the sclera," "exposing sclera by extending the conjunctival incision laterally," "cauterizing the sclera," and "placing two sutures," that the hyaluronic acid solution is used to "replace withdrawn vitreous." Without question, this disclosure destroys any argument that the hyaluronic acid solution is used prior to surgery. Furthermore, claim 8 of Balazs, which is the claim relating to surgical adhesions, specifically refers to application "during surgery or post-operatively," i.e., application before surgical manipulation is not disclosed.

In the disclosure of Balazs from column 14, line 7 ("Therapeutic Uses of Purified HUA") to column 15, line 40, it is stated, inter alia:

"Therapeutic Uses of Purified HUA

"The sterile HUA product of the invention has therapeutic application in three major areas.

"1. Prevention of fibrous tissue formation

"HUA influences the invasion and activity of cells participating in the acute and chronic inflammatory processes. Thus, the HUA of the invention can be implanted when prevention of excess fibrous tissue formation and consequent development of adhesion and scars are not desirable.

"The present HUA can also be implanted between tendons and their sheaths to minimize adhesion formation after any surgical procedure⁽²⁾.

(2) Rydell et al, Clinical Orthopaedics, No. 80, October, 1971, pps. 25-32.

"HUA can also be implanted around peripheral nerves and nerve roots after injury or surgery when damage to the connective tissue around the nerve is extensive and excessive scar formation is expected. Implantation of HUA around the healing (regenerating) nerve can protect it from invasion by connective tissue cells.

"Implantation of HUA between mesothelial, pericardial and pleural sheets and on fasciae is indicated when the prevention of adhesion formation between two endothelial or connective tissue membranes is desired.

"Implantation of HUA into the vitreous is indicated after extensive intra-vitreous surgery (removal of hemorrhages, opacities, etc.) to prevent excessive cellular reaction, and development of fibrous bands and preretinal tissue membranes.

"The aqueous humor may be replaced by HUA after various intraocular surgical procedures that might cause cellular invasion of the anterior chamber, which would endanger the regeneration and function of the iris, ciliary body and corneal endothelium.

"2. Separation of tissue surfaces with a biological prosthesis

"HUA can be used to separate tissue surfaces. The elastoviscous quality of HUA and its biological origin provide two advantages. First, it serves as a mechanical protector of the tissue during surgical manipulation and post-operatively; second, it does not cause inflammation, foreign body reaction, or development of a connective tissue capsule.

"The use of HUA as a biological prosthesis in the anterior chamber is indicated after cataract surgery in order to push back prolapsed vitreous and, after resection of the anterior face of the vitreous, to provide separation between the vitreous and cornea.

"This biological prosthesis (HUA) can be used in the anterior chamber after keratoplasty to prevent adhesion formation between the corneal wound and the iris." [Emphasis added.]

The above statements and in particular the statement that "[t]he present HUA can also be implanted between tendons and their sheaths to minimize adhesion formation after any surgical procedure" clearly shows that Balazs does not teach the application of hyaluronic acid prior to surgery to prevent adhesion formation, but only during or after surgery.

The Examiner also states that Balazs teaches the hyaluronic acid molecular weights specified in the instant claims. Balazs does not assist in teaching the molecular

weight of the hyaluronic acid solutions employed in the claimed method. Although Balazs does refer generally to hyaluronic acid having molecular weights of "at least about 750,000," the reference goes to great pains to point out that the higher the molecular weight, the better. There are numerous references throughout the patent to much higher molecular weights being preferable. At column 4, lines 44-49, it is stated that preferred molecular weights are above 1,200,000. In addition, at column 11, lines 47-55, and column 13, lines 57-67, it is stated that great care should be taken to minimize molecular weight degradation since higher molecular weights are preferable. At column 1, lines 34-37, it is stated that hyaluronic acid can have a molecular weight up to 8,000,000 (and indeed there have been reports of molecular weights in excess of 13,000,000). Thus, it appears that a skilled artisan would be taught that the reference advocates molecular weights much higher than the 1,500,000 limit imposed by the present claims.

Finally, and most critically, the only specific example in the patent to a hyaluronic solution and how to prepare it is from column 10, line 45 (Stage I) to column 13, line 54 (Stage V). At column 13, line 45, it is stated that the molecular weight is 1,586,000. Coupled with the statements in the patent that only high molecular weights are operable, it would appear that the effective lower limit of molecular weight for the hyaluronic acid of Balazs is

1,586,000 which is, of course, above the limit imposed by the present claims.

It is respectfully submitted, therefore, that Balazs is not suggestive of the claimed invention within the meaning of 35 USC §103. Accordingly, withdrawal of this ground of rejection is respectfully requested.

Applicants have earnestly endeavored to place this application in condition for allowance, and an early action toward that end is respectfully requested.

To the extent necessary, applicants petition for an extension of time under 37 CFR §1.136. Please charge any additional fees due (or credit any overpayment thereof) to Deposit Account No. 11-0610 (Docket No. 4733).

Respectfully submitted,

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